randomized between dose-escalation of the entire primary tumour or to the high FDG uptake region inside the primary tumour. Plans are normalized to the same mean lung dose, while giving 66 Gy in 24 fractions to involved lymph nodes. The trial has already accrued 66 patients and will soon be extended to five participating centres. The head and neck trial investigates the impact of delivering a high radiation dose to the most active part of the tumour, as seen on the PET-CT scan by adaptive radiotherapy. Patients are randomized between a conventional IMRT and adaptive IMRT by redistribution of the radiation dose: with higher doses given to the most active part of the tumour and low doses at the border of the CTV. In the adaptive arm, the treatment plan is modified to account for anatomical changes occurring over the course of therapy. In a factorial design, patients are randomized between 1) conventional and adaptive radiotherapy and 2) radiotherapy plus cisplatin or cetuximab. The sensitivity for cisplatin and cetuximab is estimated by both molecular profiling research and the 3D measurement of 89- Zirconium uptake in the tumour. The first patient just completed the treatment with the combination of radiotherapy and cetuximab in the head and neck cancer study. Although this is a very sophisticated and intensive approach, the treatment has proceeded without problems.

**SP-0223**

**ANDANTE: The project: a multidisciplinary approach to neutron RBE**

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There is growing concern about the possible long-term risks to radiotherapy patients from neutrons, which are generated as a by-product either in high-energy photon beams, or proton beams. The usual approach to estimating the risk from neutrons is to use ICRP risk factors and radiation weighting factors for neutrons. There are a number of problems with this, and indeed the ICRP state clearly that their numbers are approximations, which should only be used for radiation protection guidelines, and not for individuals. According to the ICRP scheme, the risk from neutrons is determined by means of the relative biological effectiveness (RBE) of neutrons compared to photons for which the risks are better known. However there is considerable uncertainty about how RBE for neutrons varies with dose and neutron energy, or whether the RBE model is even appropriate.
Two major reasons for this are that it is very difficult to obtain risk data in exposure situations where the neutron energy is confined to a narrow spectrum (or even well known), and the occurrence of risk events at the low doses of interest is very low giving poor statistics.
Previous research on risks from neutron risk has mainly been single-discipline. That is, the results have been dependent on a single experimental or epidemiological approach. By contrast, the ANDANTE project uses three different disciplines in parallel. This is analogous to taking images of an object using three different imaging modalities and combining them to produce an image much sharper than any of the individual images. The three parallel approaches are:
Physics: a track structure model is used to contrast the patterns of damage to cellular macro-molecules from neutrons compared to photons. The simulations reproduce the same energy spectra as are used in the other two approaches.
Stem cell radiobiology: stem cells from thyroid, salivary gland, and breast tissue are given well characterised exposures to neutrons and photons. A number of endpoints are used to estimate the relative risk of damage from neutrons compared to photons. As well, irradiated cells will be transplanted into mice to investigate the incidence of progression into tumours.
Epidemiology: the relative incidence rates of second cancers of the thyroid, salivary gland, and breast following paediatric radiotherapy (conventional radiotherapy for photons and proton therapy for neutrons) are investigated in a pilot single-institution study, leading to a multi-institution prospective study.
The project has completed the first of its four years. Progress on characterising the exposure beams, isolation and initial exposures of stem cells, and data collection for the epidemiological studies will be presented.

**SP-0224**

**ANDANTE: Radiation induced carcinogenesis of salivary and thyroid gland stem cells**

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Out-of field neutron exposure of proton therapy might lead to enhanced formation of second cancer. The goal of the Andante project is to estimate the risk of second cancer from out-of field neutron exposure and compare this with other treatment modalities. This study focuses on two specific cancers that may be detected as second malignant neoplasms following pediatric radiotherapy:salivary gland and thyroid gland cancer. It has been suggested that adult stem cells are a critical target for radiation carcinogenesis. Therefore, in this study adult stem cells from murine salivary and thyroid glands were isolated and expanded in culture. Stem cell containing spheroids (multicellular 3D structures) could be obtained from both murine salivary and thyroid glands in non-adherent cultivation of cell suspensions of salivary and thyroid gland tissue in serum-free conditions. After digestion of spheroids into single cells, cells were exposed to different doses (0.1, 0.5, 1, 2, 5 Gy) of $\Upsilon$-irradiation. To determine transformation, *in vitro* self-renewal and differentiation capacity were investigated of irradiated cells and were compared to unirradiated cells. In addition, salivary and thyroid cells were isolated from inducible p53 knockout mice to test the carcinogenesis potential of the model. Transplantation of irradiated stem cells in photon-irradiated salivary glands will be performed to get information on carcinogenic transformation *in vivo*. In the future, stem cells will be exposed to neutrons and will be compared to the exposure of photons.

## POSTER DISCUSSION: 6: PHYSICS: DOSE MEASUREMENTS

**PD-0225**

**IMRT credentialing for prospective trials using institutional phantoms: Results of a joint EORTC and RPC project.**

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**Purpose/Objective:** Intensity-modulated radiotherapy (IMRT) credentialing for the 22074-24071 Head and Neck (H&N) EORTC study was performed using the anthropomorphic head phantom from the Radiological Physics Center (RPC; $RPC_{ph}$). Institutions were also retrospectively requested to irradiate their own in-house phantom ($Inst_{ph}$) using the same treatment plan in the framework of a Virtual Phantom Project (VPP) for IMRT credentialing. Both measurement and calculations for the $RPC_{ph}$ and $Inst_{ph}$ were sent to the EORTC for central analysis using the digital quality assurance (QA) platform.
**Materials and Methods:** Calculated and measured 2D dose matrices on the $Inst_{ph}$ were requested from centers and send to a dedicated secured EORTC uploader. RPC analyzed the credentialing measurements performed in the $RPC_{ph}$ using the VPP metrics. Data from the $RPC_{ph}$ and $INST_{ph}$ were thereafter centrally analyzed and inter-compared by the QA team using commercially available software.
**Results:** Eighteen institutions participated to the VPP. The measurements of 6 (33%) institutions could not be analyzed centrally, as a result of incomplete datasets (*n*=4) or dose-matrix format issues (*n*=2). All other centers (*n*=12; 66%) could be credentialed successfully using the VPP protocol and the dose-gradient produced by the IMRT plans were acceptable in all cases using the RPC criteria. The same number of institutions (*n*=12) was successfully credentialed using the more stringent 5%/5 mm pass at the 90% pixel cutoff-level gamma analysis criteria. A passing rate of 84.8±13.1%, 97.8±3.2% and 99.3±1.2% for the 3%/3 mm,5%/5 mm and 7%/4mm QA criteria, respectively, was observed with $RPC_{ph}$. A corresponding passing rate of 93.5±5.4%, 98.9±1.5% and 99.4±1.2% for 3%/3 mm, 5%/5 mm and 7%/4mm QA criteria , respectively, was observed with the VPP using $Inst_{ph}$ data.
**Conclusions:** IMRT credentialing for H&N prospective trials using institutional phantom measurements is possible and was successful in all cases using the RPC passing criteria.

**PD-0226**

**New robotic phantom: Evaluation of performance in radiotherapy**

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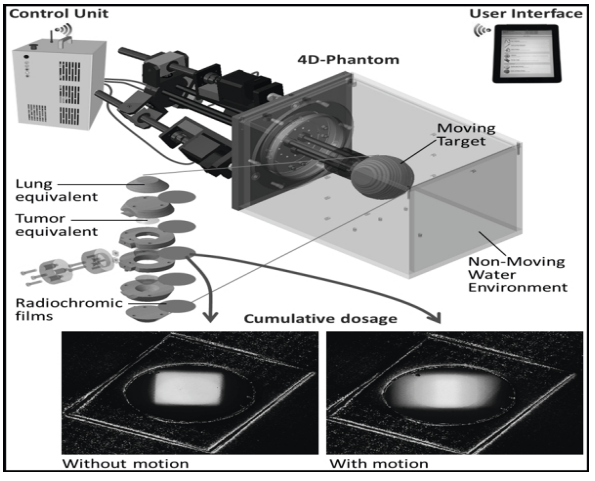
**Purpose/Objective:** Techniques in radiotherapy that account for the effects of motion of the target tissue, have gained increasing importance in both research and clinical practice. Validation of these techniques requires robotic phantoms, which represent structure, physical properties and motion of a human body environment and allow dose measurement. Such phantom was recently developed by our group. It allows generation respectively reproduction of previously recorded patient motion in all translational degrees of freedom with sub-millimeter precision while featuring a realistic structural design, which involves the relative motion of an inside tumour with respect to a static environment as well as an extensive modularization of tissue equivalent components and dosage measurement devices. The objective of this work is to evaluate the applicability of the novel robotic phantom in clinical practice of quality insurance of radiotherapy and assess the phantom's potentials.
**Materials and Methods:** A solid perplex sphere, encased by a layer of wood was used to resemble the tissues of the target of dose application and the surrounding lung. Radiochromic films, placed in five cutting planes of the sphere, were used for dose measurements. The sphere was attached to a flange moving in a water environment. Irradiation with different field forms was applied on the robotic phantom, first, with its actuators blocked, then, with concurrent playback of respiratory motion. Dose distributions measured and calculated by the treatment planning system (TPS) were compared.
**Results:** Application of the phantom in both medical imaging and radiotherapy and obtained results have proven feasible. The construction turned out not to cause any noticable distortions, e.g. as a result of the robotic components of the phantom. In static case, measured and calculated dose distributions were compared with Gamma Index criteria (3mm/3%). All evaluated films agreed with the calculated dose distribution with an accordance above 99%. Dose distributions measured with the moving phantom showed typical dose blurring. The system components of the robotic phantom and test results are depicted in the figure.




**Conclusions:** Suitability of the physical properties of the robotic phantom, applicability in clinical practice and capability of validation of the process chain of radiotherapy in the presence of motion with a realistic setup and test scenario were successfully proven. The new features of the robotic phantom, e.g. the uniquely high customizability of both motion and structure of the human body replication will allow the effects of motion to be comprehensively investigated and techniques of motion compensation to be improved in the future.

**PD-0227**
**Verification of dose painting and target tracking with a 3D dosimetry system**
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**Purpose/Objective:** The increasing complexity of radiotherapy (RT) has motivated research into three dimensional (3D) dosimetry. In this study we investigate the use of 3D dosimetry with polymerizing gels and optical computed tomography (optical CT) as a verification tool for complex RT: dose painting, and target tracking.

**Materials and Methods:** For the dose painting studies, two dosimeters were irradiated with a 7-field intensity modulated radiotherapy (IMRT) plan with and without dose prescription based on a hypoxia image dataset of a head and neck patient. In the tracking experiments, two dosimeters were irradiated with a volumetric modulated arc therapy (VMAT) plan with and without clinically measured prostate motion and a third with both motion and target tracking. To assess the performance, 3D gamma analyses were performed between measured and calculated stationary dose distributions.
**Results:** Gamma pass-rates of 95.3 % and 97.3 % (figure 1) were achieved for the standard and dose-painted IMRT plans. Gamma pass-rates of 91.4 % and 54.4 % were obtained for the stationary and moving dosimeter, respectively, while tracking increased the pass-rate for the moving dosimeter to 90.4 %.

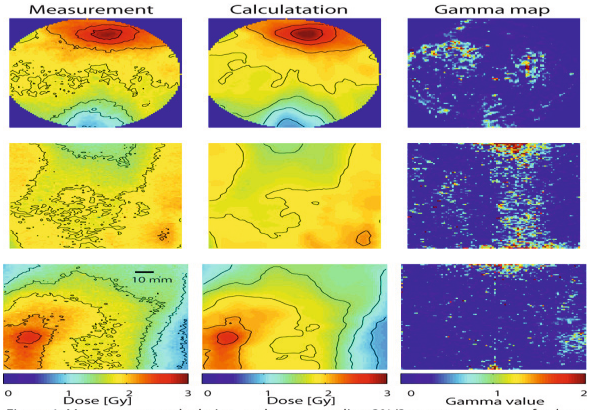

Figure 1: Measurement, calculation, and corresponding 3%/3mm gamma map of a dose painted IMRT delivery. The 3D distribution is viewed in the transversal (upper row), coronal (middle row), and sagittal plane (bottom row). A gamma pass-rate above 97 % was obtained.

**Conclusions:** This study has shown that the 3D dosimetry system can reproduce and thus verify complex dose distributions, also when influenced by motion.

**PD-0228**
**Dose-guided radiotherapy for prostate cancer patients; implications of intra-fraction anatomy variations.**
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**Purpose/Objective:** In dose-guided radiotherapy, delivered fluence may be adapted based on the actual delivered patient dose in previous fractions, as derived from in-room acquired cone-beam CTs (CBCTs) and electronic portal images (EPIs).In our institute, EPIs are converted into absolute portal dose images (PDIs), and compared to PDI predictions to assess the actual delivered 2D fluence profiles. PDI predictions are based on segment shapes and MUs stored in the linac R&V system and the fraction CBCT. Estimated actual delivered fluences and the CBCT might then be used to reconstruct the delivered 3D patient dose in a fraction. In case of intra-fraction anatomy changes, the CBCT may not accurately represent the patient anatomy for all treatment beams, yielding inaccuracies in reconstructed patient dose. Here we will focus on the impact of intra-fraction motion on the accuracy of estimated fluence profiles used in the patient dose reconstruction.
**Materials and Methods:** For 50 prostate cancer patients treated with 5-7 IMRT fields, CBCTs and EPIs were acquired in 4-5 fractions. PDIs derived from EPIs were compared to predictions based on the CBCT. To accurately predict beam transmission, Hounsfield units from the planning CT-scan were mapped onto the CBCT while accounting for the patient's non-rigid anatomy, using our previously published algorithm. Predictions also accounted for treatment couch absorption, using our recently published couch model. As benchmark, measured and predicted PDIs were also compared for an anatomical phantom, irradiated with the plans of 10 patients. Gamma-analyses with 3% global dose difference and 3 mm distance to agreement as reference criteria were performed. Combination of fractions was evaluated to enhance the accuracy of estimated delivered fluence profiles.
**Results:** For the phantom, the average percentage of rejected pixels in PDIs was 0.8±0.7% (1SD). For the 1413 evaluated patient fields this increased to 1.4 ± 2.8%. The increase could partially be attributed to intra-fraction anatomy changes. Due to these changes, the acquired CBCT was not fully representative for all fields. For some fractions this resulted in large differences between fields in agreement between measured and predicted PDI. Combination of the first 2 fractions yielded results in close agreement with the phantom (average percentage of rejected pixels: 0.6 ±3.4%).The agreement